

and insert the following therefor as a separate page after the claims:

-Abstract of the Disclosure

A
Compounds are disclosed having the general formula R₁-X-R₂, wherein R₁ and R₂ are biologically active groups, at least one of which is polypeptidic. X is a non-peptidic polymeric group. R₁ and R₂ may be the same or different. Preferred R₁ and R₂ groups are TNF inhibitors.

In the Claims

Please delete claims 1-14 and 16-44, without prejudice or disclaimer.

Please amend claim 15, as follows:

A²
15. A [substantially purified] compound of the formula R₁-X-R₂, wherein:

[X comprises a non-peptidic polymer having a first reactive group and a second reactive group, wherein said first reactive group is a Michael acceptor; and]

R₁ and R₂ are each a tumor necrosis factor (TNF) inhibitor polypeptide selected from:

(a) 30 kDa TNF inhibitor or 40 kDa TNF inhibitor,

(b) 30 kDa TNF inhibitor or 40 kDa TNF inhibitor, modified to contain at least one non-native cysteine residue, and

(c) a biologically active portion of (a) or (b), wherein R₁ and R₂ bind to TNF; and

[comprises a biologically-active molecule having a reactive thiol moiety, said biologically-active molecule is covalently bonded to said non-peptidic polymer by reaction of said thiol moiety with said Michael acceptor, and said biologically-active molecule retains its biological activity after said reaction; and

R₂ comprises a biologically-active molecule or a nonbiologically-active group bonded to said non-peptidic polymer by reaction with said second reactive group]

X is a non-peptidic polymer having two activated groups linked thereto, said non-peptidic polymer being selected from polyethylene glycol, polypropylene glycol, polyoxyethylated glycerol and other polyoxyethylated polyols, polyvinyl alcohol and other polyalkylene oxides, polyoxyethylated sorbitol or polyoxyethylated glucose.

A³
Please add the following new claims:

47. The compound of claim 15, wherein R₁ and R₂ are identical.

- A, 3
Cont.*
3. The compound of claim ~~15~~, wherein R₁ and R₂ are different.
4. The compound of claim ~~15~~, wherein R₁ and R₂ are said 30 kDa TNF inhibitor.
5. The compound of claim ~~41~~, wherein said 30 kDa TNF inhibitor is modified to contain at least one non-native cysteine residue.
6. The compound of claim ~~48~~, wherein said non-native cysteine residue is found at an amino acid residue site selected from the group consisting of 1, 14, 105, 111 and 165.
7. The compound of claim ~~15~~, wherein R₁ and R₂ are each a portion of said 30 kDa TNF inhibitor.
8. The compound of claim ~~15~~, wherein R₁ and R₂ are covalently bonded to X by thio-ether bonds.
9. The compound of claim ~~51~~, wherein cysteine residues of R₁ and R₂ are part of said thio-ether bonds.
10. The compound of claim ~~15~~, wherein R₁ and R₂ are attached to said polyethylene glycol via a cysteine residue.
11. A pharmaceutical composition comprised of an effective amount of the compound of claim ~~15~~ in a pharmacologically acceptable carrier.
12. The compound of claim ~~15~~, which has been prepared by a method comprising simultaneously reacting R₁ and R₂ with X, wherein X has at least two reactive groups capable of forming thio-ether bonds when reacted with cysteine amino acid residues.
13. The compound of claim ~~58~~, wherein R₁ and R₂ are said 30 kDa TNF inhibitor or a portion thereof, modified to contain a non-native cysteine residue.
14. The compound of claim ~~15~~, which has been prepared by a method comprising reacting R₁ with X to form a complex R₁-X and subsequently reacting said complex R₁-X with R₂ to form the compound R₁-X-R₂, wherein X has at least two reactive groups capable of forming thio-ether bonds when reacted with cysteine amino acid residues.
15. The compound of claim ~~51~~, wherein R₁ and R₂ are said 30 kDa TNF inhibitor or a portion thereof, modified to contain a non-native cysteine residue.